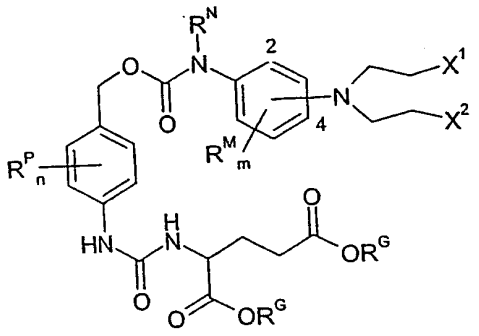
CLAIMS

1. A compound of the formula:



(1)

wherein:

R^N is independently C_{1-7}alkyl;

X^1 is independently -I, -Br, or -Cl;

X^2 is independently -I, -Br, or -Cl;

the group $-N(CH_2CH_2X^1)(CH_2CH_2X^2)$ is independently attached at the 2-position or at the 4-position;

each R^G is independently -H or an ester substituent;

n is independently an integer from 0 to 4;

each R^P, if present, is independently a phenyl substituent;

m is independently an integer from 0 to 4;

each R^M, if present, is independently a mustard substituent;

and pharmaceutically acceptable salts, solvates, amides, and esters thereof.

* * *

2. A compound according to claim 1, wherein R^N is independently aliphatic C_{1-7}alkyl.

3. A compound according to claim 1, wherein R^N is independently unsubstituted C_{1-7}alkyl.

4. A compound according to claim 1, wherein R^N is independently unsubstituted aliphatic C_{1-7}alkyl.

5. A compound according to claim 1, wherein R^N is independently C_{1-4}alkyl.

6. A compound according to claim 1, wherein R^N is independently aliphatic C_{1-4}alkyl.

7. A compound according to claim 1, wherein R^N is independently unsubstituted C_{1-4}alkyl.

8. A compound according to claim 1, wherein R^N is is independently unsubstituted aliphatic C_{1-4}alkyl.

9. A compound according to claim 1, wherein R^N is is independently -Me, -Et, -nPr, -iPr, -allyl, -nBu, -sBu, -iBu, or -tBu.

10. A compound according to claim 1, wherein R^N is is independently -Me or -Et.

11. A compound according to claim 1, wherein R^N is is independently -Me.

* * *

12. A compound according to any one of claims 1 to 11, wherein each of X^1 and X^2 is independently -I, -Br, or -Cl; and both of X^1 and X^2, are the same.

13. A compound according to any one of claims 1 to 11, wherein each of X^1 and X^2 is independently -I or -Br.

14. A compound according to any one of claims 1 to 11, wherein each of X^1 and X^2 is independently -I or -Br; and both of X^1 and X^2 are the same.

15. A compound according to any one of claims 1 to 11, wherein each of X^1 and X^2 is independently -I.

16. A compound according to any one of claims 1 to 11, wherein each of X^1 and X^2 is independently -Br.

17. A compound according to any one of claims 1 to 11, wherein each of X^1 and X^2 is independently -Cl.

* * *

18. A compound according to claim 1, wherein
R^N is independently C_{1-4}alkyl; and,
each X is independently -Cl, -Br or -I.

19. A compound according to claim 1, wherein
R^N is independently -Et or -Me; and,
each X is independently -Cl, -Br or -I.

20. A compound according to claim 1, wherein
R^N is independently -Me; and,
each X is independently -Cl, -Br or -I.

21. A compound according to claim 1, wherein
R^N is independently C_{1-4}alkyl; and,
each X is independently -Br or -I.

22. A compound according to claim 1, wherein
R^N is independently -Et or -Me; and,
each X is independently -Br or -I.

23. A compound according to claim 1, wherein
R^N is independently -Me; and,
each X is independently -Br or -I.

24. A compound according to claim 1, wherein
R^N is independently C_{1-4}alkyl; and,
each X is independently -I.

25. A compound according to claim 1, wherein
R^N is independently -Et or -Me; and,
each X is independently -I.

26. A compound according to claim 1, wherein
R^N is independently -Me; and,
each X is independently -I.

* * *

27. A compound according to any one of claims 1 to 26, wherein the group $-N(CH_2CH_2X^1)(CH_2CH_2X^2)$ is independently attached at the 4-position.

* * *

28. A compound according to claim 1, wherein
R^N is independently C_{1-4}alkyl;
each X is independently -Cl, -Br or -I; and,
the group $-N(CH_2CH_2X)_2$ is independently attached at the 4-position.

29. A compound according to claim 1, wherein
R^N is independently -Et or -Me;
each X is independently -Cl, -Br or -I; and,
the group $-N(CH_2CH_2X)_2$ is independently attached at the 4-position.

30. A compound according to claim 1, wherein
R^N is independently -Me;
each X is independently -Cl, -Br or -I; and,
the group $-N(CH_2CH_2X)_2$ is independently attached at the 4-position.

31. A compound according to claim 1, wherein
R^N is independently C_{1-4}alkyl;
each X is independently -Br or -I; and,
the group $-N(CH_2CH_2X)_2$ is independently attached at the 4-position.

32. A compound according to claim 1, wherein
R^N is independently -Et or -Me;
each X is independently -Br or -I; and,
the group $-N(CH_2CH_2X)_2$ is independently attached at the 4-position.

33. A compound according to claim 1, wherein
R^N is independently -Me;
each X is independently -Br or -I; and,
the group $-N(CH_2CH_2X)_2$ is independently attached at the 4-position.

34. A compound according to claim 1, wherein
R^N is independently C_{1-4}alkyl;
each X is independently -I; and,
the group $-N(CH_2CH_2X)_2$ is independently attached at the 4-position.

35. A compound according to claim 1, wherein
R^N is independently -Et or -Me;
each X is independently -I; and,
the group $-N(CH_2CH_2X)_2$ is independently attached at the 4-position.

36. A compound according to claim 1, wherein
R^N is independently -Me;
each X is independently -I; and,
the group $-N(CH_2CH_2X)_2$ is independently attached at the 4-position.

* * *

37. A compound according to any one of claims 1 to 36, wherein n is 0, 1, or 2.

38. A compound according to any one of claims 1 to 36, wherein n is 0 or 1.

39. A compound according to any one of claims 1 to 36, wherein n is 2.

40. A compound according to any one of claims 1 to 36, wherein n is 1.

41. A compound according to any one of claims 1 to 36, wherein n is 0.

* * *

42. A compound according to any one of claims 1 to 41, wherein each R^P, if present, is independently halo, C_{1-4}alkyl, nitro, or cyano.

43. A compound according to any one of claims 1 to 41, wherein each R^P, if present, is independently:
-F, -Cl, -Br, -I, -Me, -Et, -nPr, -iPr, -nBu, -sBu, -iBu, -tBu, $-NO_2$, or -CN.

44. A compound according to any one of claims 1 to 41, wherein each R^P, if present, is independently -F, -Cl, -Br, or -I.

45. A compound according to any one of claims 1 to 41, wherein each R^P, if present, is independently -F, -Cl or -Br.

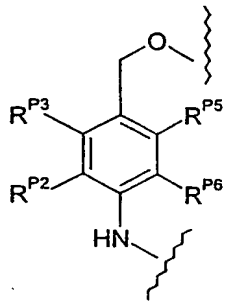
46. A compound according to any one of claims 1 to 41, wherein each R^P, if present, is independently -F or -Cl.

47. A compound according to any one of claims 1 to 41, wherein each R^P, if present, is independently -F or -Br.

48. A compound according to any one of claims 1 to 41, wherein each R^P, if present, is independently -F.

* * *

49. A compound according to any one of claims 1 to 48, wherein the phenylene group has the following formula:



wherein each of R^{P2}, R^{P3}, R^{P5}, and R^{P6} is independently -H, halo, C_{1-4}alkyl, nitro, or cyano.

50. A compound according to claim 49, wherein each of R^{P2} and R^{P6} is -H; and each of R^{P3} and R^{P5} is independently halo, C_{1-4}alkyl, nitro, or cyano.

51. A compound according to claim 49, wherein each of R^{P2}, R^{P5}, and R^{P6} is -H; and R^{P3} is independently halo, C_{1-4}alkyl, nitro, or cyano.

52. A compound according to claim 49, wherein each of R^{P2}, R^{P3}, R^{P5}, and R^{P6} is -H.

* * *

53. A compound according to any one of claims 1 to 52, wherein m is 0, 1, or 2.

54. A compound according to any one of claims 1 to 52, wherein m is 0 or 1.

55. A compound according to any one of claims 1 to 52, wherein m is 2.

56. A compound according to any one of claims 1 to 52, wherein m is 1.

57. A compound according to any one of claims 1 to 52, wherein m is 0.

* * *

58. A compound according to any one of claims 1 to 57, wherein each R^M, if present, is independently selected from: C_{1-4}alkyl; C_{1-4}alkoxy; amino; halo; C_{1-4}alkylthio; acyl; ester; amido; cyano; nitro; and, C_{5-6}aryl.

59. A compound according to any one of claims 1 to 57, wherein each R^M, if present, is independently selected from:

-Me, -Et, -nPr, -iPr, -nBu, -sBu, -iBu, -tBu;
$-CF_3$, $-CH_2F$, $-CH_2CF_3$, $-CH_2CH_2F$; $-CF_2CF_3$;
-OMe, -OEt, -O-nPr, -O-iPr, -O-nBu, -O-sBu, -O-iBu, -O-tBu;
$-OCF_3$, $-OCH_2F$, $-OCH_2CF_3$, $-OCH_2CH_2F$; $-OCF_2CF_3$;
$-NH_2$, $-NMe_2$, $-NEt_2$, $-N(nPr)_2$, $-N(iPr)_2$,
-F, -Cl, -Br, -I;
-SMe, -SEt;
-C(=O)Me;
-C(=O)OMe, -C(=O)OEt;
$-CONH_2$, -CONHMe;
-CN;
$-NO_2$; and,
-Ph.

60. A compound according to any one of claims 1 to 57, wherein each R^M, if present, is independently selected from:

C_{1-4}alkyl; C_{1-4}alkoxy; and, amino.

61. A compound according to any one of claims 1 to 57, wherein each R^M, if present, is independently selected from:

-Me, -Et, -nPr, -iPr, -nBu, -sBu, -iBu, -tBu;

$-CF_3$, $-CH_2F$, $-CH_2CF_3$, $-CH_2CH_2F$; $-CF_2CF_3$;

-OMe, -OEt, -O-nPr, -O-iPr, -O-nBu, -O-sBu, -O-iBu, -O-tBu;

$-OCF_3$, $-OCH_2F$, $-OCH_2CF_3$, $-OCH_2CH_2F$; $-OCF_2CF_3$;

$-NH_2$, $-NMe_2$, $-NEt_2$, $-N(nPr)_2$, and $-N(iPr)_2$,

62. A compound according to any one of claims 1 to 57, wherein each R^M, if present, is independently selected from:

-Me, -Et, $-CF_3$, -OMe, -OEt, $-NH_2$, and $-NMe_2$.

* * *

63. A compound according to any one of claims 1 to 62, wherein each R^G is independently -H.

* * *

64. A compound according to any one of claims 1 to 62, wherein each R^G is independently -H, unsubstituted C_{1-7}alkyl, substituted C_{1-7}alkyl, or silyl.

65. A compound according to any one of claims 1 to 62, wherein each R^G is independently -H, unsubstituted C_{1-7}alkyl, or substituted C_{1-7}alkyl.

66. A compound according to any one of claims 1 to 62, wherein each R^G is independently -H or unsubstituted C_{1-7}alkyl.

* * *

67. A compound according to any one of claims 64 to 66, wherein the unsubstituted C_{1-7}alkyl group is independently unsubstituted C_{1-4}alkyl.

68. A compound according to any one of claims 64 to 66, wherein the unsubstituted C_{1-7}alkyl group is independently: -Me, -Et, -nPr, -iPr, -allyl, -nBu, -sBu, -iBu, or -tBu.

* * *

69. A compound according to claim 64 or claim 65, wherein the substituted C_{1-7}alkyl group is independently C_{1-7}alkyl substituted with one or more groups selected from optionally substituted C_{5-20}aryl, C_{1-7}alkoxy, C_{1-7}alkylthio, and acyloxy.

70. A compound according to claim 64 or claim 65, wherein the substituted C_{1-7}alkyl group is independently C_{1-4}alkyl substituted with one or more groups selected from optionally substituted C_{5-20}aryl, C_{1-7}alkoxy, C_{1-7}alkylthio, and acyloxy.

71. A compound according to claim 64 or claim 65, wherein the substituted C_{1-7}alkyl group is independently C_1alkyl substituted with one or more groups selected from optionally substituted C_{5-20}aryl, C_{1-7}alkoxy, C_{1-7}alkylthio, and acyloxy.

72. A compound according to claim 64 or claim 65, wherein the substituted C_{1-7}alkyl group is independently C_{1-7}alkyl substituted with one or more groups selected from optionally substituted C_{5-6}aryl, C_{1-4}alkoxy, C_{1-4}alkylthio, C_{1-4}alkyl-acyloxy, C_{5-6}aryl-acyloxy.

73. A compound according to claim 64 or claim 65, wherein the substituted C_{1-7}alkyl group is independently C_{1-4}alkyl substituted with one or more groups selected from optionally substituted C_{5-6}aryl, C_{1-4}alkoxy, C_{1-4}alkylthio, C_{1-4}alkyl-acyloxy, C_{5-6}aryl-acyloxy.

74. A compound according to claim 64 or claim 65, wherein the substituted C_{1-7}alkyl group is independently C_1alkyl substituted with one or more groups selected from optionally substituted C_{5-6}aryl, C_{1-4}alkoxy, C_{1-4}alkylthio, C_{1-4}alkyl-acyloxy, C_{5-6}aryl-acyloxy.

75. A compound according to claim 64 or claim 65, wherein the substituted C_{1-7}alkyl group is independently C_{1-7}alkyl substituted with one or more groups selected from optionally substituted phenyl (e.g., methoxyphenyl, nitrophenyl), methoxy, methylthio, acetoxy, and benzoyloxy.

76. A compound according to claim 64 or claim 65, wherein the substituted C_{1-7}alkyl group is independently C_{1-4}alkyl substituted with one or more groups selected from optionally substituted phenyl (e.g., methoxyphenyl, nitrophenyl), methoxy, methylthio, acetoxy, and benzoyloxy.

77. A compound according to claim 64 or claim 65, wherein the substituted C_{1-7}alkyl group is independently C_1alkyl substituted with one or more groups selected from optionally substituted phenyl (e.g., methoxyphenyl, nitrophenyl), methoxy, methylthio, acetoxy, and benzoyloxy.

* * *

78. A compound according to claim 64, wherein the silyl group is independently $-SiR^S_3$, wherein each R^S is independently -H or C_{1-4}alkyl.

79. A compound according to claim 64, wherein the silyl group is independently $-Si(Me)_3$, $-Si(Et)_3$, $-Si(iPr)_3$, $-Si(tBu)(CH_3)_2$, or $-Si(tBu)_3$.

80. A compound according to claim 64, wherein the silyl group is independently $-Si(iPr)_3$.

* * *

81. A compound according to any one of claims 1 to 62, wherein each R^G is independently (1) t-butyl, (2) allyl, (3) tri-isopropylsilyl, (4) acetoxymethyl, (5) methoxymethyl, (6) methylthiomethyl, (7) p-methoxyphenylmethyl, (8) bis(o-nitrophenyl)methyl, (9) benzyl, or (10) diphenylmethyl.

82. A compound according to any one of claims 1 to 62, wherein each R^G is independently (1) t-butyl, (2) allyl, (3) tri-isopropylsilyl, (4) acetoxymethyl, or (5) methoxymethyl.

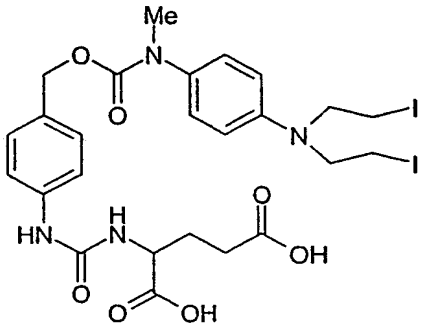
83. A compound according to any one of claims 1 to 62, wherein each R^G is independently (1) t-butyl, (2) allyl, or (3) tri-isopropylsilyl.

84. A compound according to any one of claims 1 to 62, wherein each R^G is independently (1) t-butyl or (2) allyl.

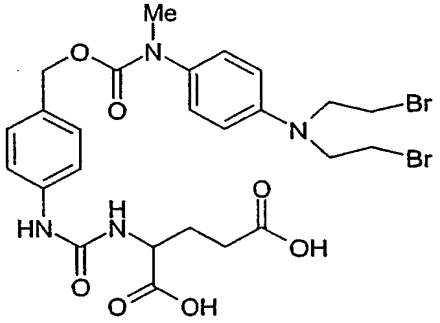
85. A compound according to any one of claims 1 to 62, wherein each R^G is independently (1) allyl.

* * *

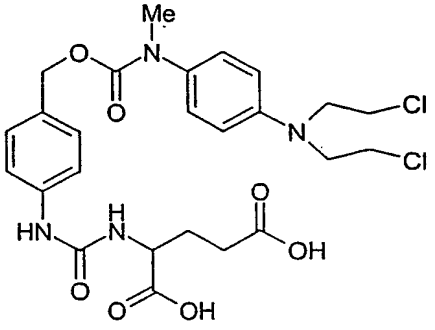
86. A compound selected from compounds of the following formula (P-1), and pharmaceutically acceptable salts, solvates, amides, and esters thereof:



87. A compound selected from compounds of the following formula (P-2), and pharmaceutically acceptable salts, solvates, amides, and esters thereof:



88. A compound selected from compounds of the following formula (P-3), and pharmaceutically acceptable salts, solvates, amides, and esters thereof:



* * *

89. A composition comprising a compound according to any one of claims 1 to 88, and a carrier.

90. A composition comprising a compound according to any one of claims 1 to 88, and a pharmaceutically acceptable carrier.

* * *

91. A method of (a) regulating proliferation of a cell; (b) inhibiting cell cycle progression of a cell; (c) promoting apoptosis of a cell; or (d) a combination of one or more of these, *in vitro* or *in vivo,* comprising contacting the cell with an effective amount of a compound according to any one of claims 1 to 90.

92. A method of regulating proliferation of a cell, *in vitro* or *in vivo,* comprising contacting the cell with an effective amount of a compound according to any one of claims 1 to 90.

93. A method of treatment of a proliferative condition comprising administering to a subject in need of treatment a therapeutically-effective amount of a compound according to any one of claims 1 to 90.

94. A method of treatment of cancer comprising administering to a subject in need of treatment a therapeutically-effective amount of a compound according to any one of claims 1 to 90.

* * *

95. A compound according to any one of claims 1 to 90, for use in a method of treatment of the human or animal body by therapy.

96. A compound according to any one of claims 1 to 90, for use in a method of treatment of a proliferative condition of the human or animal body by therapy.

97. A compound according to any one of claims 1 to 90, for use in a method of treatment of cancer of the human or animal body by therapy.

* * *

98. Use of a compound according to any one of claims 1 to 90 for the manufacture of a medicament for the treatment of a proliferative condition.

99. Use of a compound according to any one of claims 1 to 90 for the manufacture of a medicament for the treatment of cancer.

* * *

100. A kit comprising:

(a) a compound according to any one of claims 1 to 90; and

(b) instructions for use.

* * *

101. A method of (a) regulating proliferation of a cell; (b) inhibiting cell cycle progression of a cell; (c) promoting apoptosis of a cell; or (d) a combination of one or more of these, *in vitro* or *in vivo,* comprising contacting the cell with a therapeutically-effective amount of a compound according to any one of claims 1 to 90, in the presence of a carboxypeptidase enzyme.

102. A method of regulating proliferation of a cell, *in vitro* or *in vivo,* comprising contacting the cell with a therapeutically-effective amount of a compound according to any one of claims 1 to 90, in the presence of a carboxypeptidase enzyme.

103. A method of treatment of a proliferative condition comprising administering to a subject in need of treatment a therapeutically-effective amount of a compound according to any one of claims 1 to 90, in the presence of a carboxypeptidase enzyme.

104. A method of treatment of cancer comprising administering to a subject in need of treatment a therapeutically-effective amount of a compound according to any one of claims 1 to 90, in the presence of a carboxypeptidase enzyme.

* * *

105. A two component system comprising:

(a) a compound according to any one of claims 1 to 90; and,

(b) an antibody or fragment thereof conjugated or fused to a carboxypeptidase enzyme.

106. A two component system comprising:

(a) a compound according to any one of claims 1 to 90; and,

(b) an antibody or fragment thereof conjugated or fused to a carboxypeptidase enzyme,

for use in a method of treatment of the human or animal body by therapy.

* * *

107. Use of a two component system comprising:

(a) a compound according to any one of claims 1 to 90; and,

(b) an antibody or fragment thereof conjugated or fused to a carboxypeptidase enzyme,

for the manufacture of a medicament for the treatment of a proliferative condition.

108. Use of a two component system comprising:

(a) a compound according to any one of claims 1 to 90; and,

(b) an antibody or fragment thereof conjugated or fused to a carboxypeptidase enzyme,

for the manufacture of a medicament for the treatment of cancer.

* * *

109. A kit comprising:

(a) a compound according to any one of claims 1 to 90;

(b) an antibody or fragment thereof conjugated or fused to a carboxypeptidase enzyme; and,

(c) instructions for use.

* * *

110. A method of (a) regulating proliferation of a cell; (b) inhibiting cell cycle progression of a cell; (c) promoting apoptosis of a cell; or (d) a combination of one or more of these, *in vitro* or *in vivo,* comprising:

(i) contacting the cell with an antibody or fragment thereof conjugated or fused to a carboxypeptidase enzyme; and,

(ii) contacting the cell with a therapeutically-effective amount of a compound according to any one of claims 1 to 90.

111. A method of regulating proliferation of a cell, *in vitro* or *in vivo,* comprising:

(i) contacting the cell with an antibody or fragment thereof conjugated or fused to a carboxypeptidase enzyme; and,

(ii) contacting the cell with a therapeutically-effective amount of a compound according to any one of claims 1 to 90.

112. A method of treatment of a proliferative condition, comprising administering to a subject in need of treatment:

(i) an antibody or fragment thereof conjugated or fused to a carboxypeptidase enzyme; and,

(ii) contacting the cell with a therapeutically-effective amount of a compound according to any one of claims 1 to 90.

113. A method of treatment of cancer, comprising administering to a subject in need of treatment:

(i) an antibody or fragment thereof conjugated or fused to a carboxypeptidase enzyme; and,

(ii) contacting the cell with a therapeutically-effective amount of a compound according to any one of claims 1 to 90.

* * *

114. A two component system comprising:

(a) a compound according to any one of claims 1 to 90; and,

(b) a nucleic acid encoding a carboxypeptidase enzyme.

115. A two component system comprising:

(a) a compound according to any one of claims 1 to 90; and,

(b) a nucleic acid encoding a carboxypeptidase enzyme,

for use in a method of treatment of the human or animal body by therapy.

* * *

116. Use of a two component system comprising:

(a) a compound according to any one of claims 1 to 90; and,

(b) a nucleic acid encoding a carboxypeptidase enzyme,

for the manufacture of a medicament for the treatment of a proliferative condition.

117. Use of a two component system comprising:

(a) a compound according to any one of claims 1 to 90; and,

(b) a nucleic acid encoding a carboxypeptidase enzyme,

for the manufacture of a medicament for the treatment of cancer.

* * *

118. A kit comprising:

(a) a compound according to any one of claims 1 to 90;

(b) a nucleic acid encoding a carboxypeptidase enzyme; and,

(c) instructions for use.

* * *

119. A method of (a) regulating proliferation of a cell; (b) inhibiting cell cycle progression of a cell; (c) promoting apoptosis of a cell; or (d) a combination of one or more of these, *in vitro* or *in vivo,* comprising:

(i) contacting the cell with a nucleic acid encoding a carboxypeptidase enzyme; and,

(ii) contacting the cell with a therapeutically-effective amount of a compound according to any one of claims 1 to 90.

120. A method of regulating proliferation of a cell, *in vitro* or *in vivo,* comprising:

(i) contacting the cell with a nucleic acid encoding a carboxypeptidase enzyme; and,

(ii) contacting the cell with a therapeutically-effective amount of a compound according to any one of claims 1 to 90.

121. A method of treatment of a proliferative condition, comprising administering to a subject in need of treatment:

(i) a nucleic acid encoding a carboxypeptidase enzyme; and,

(ii) a therapeutically-effective amount of a compound according to any one of claims 1 to 90.

122. A method of treatment of cancer, comprising administering to a subject in need of treatment:

(i) a nucleic acid encoding a carboxypeptidase enzyme; and,

(ii) a therapeutically-effective amount of a compound according to any one of claims 1 to 90.